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Online Availability of Fish Antibiotics and Documented Intent for Self-Medication

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Online availability of fish antibiotics and documented intent for self-medication

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Abstract

Self-medication and antibiotic utilization without healthcare oversight may lead to delayed appropriate treatment, transmission of communicable infections, untoward adverse events, and contribute to antimicrobial resistance. Previous data suggest people obtain over-the-counter (OTC) animal antibiotics for their personal use. This study examined the availability of OTC fish antibiotics online and the documented intent for self-medication. The authors conducted a web-based cross-sectional study using Google search engine to identify vendor websites selling fish antibiotics in the United States. Vendor websites were included if product information, consumer reviews, and comments were publicly available. Nine fish antibiotics were chosen due to their possibility of having consequences to human misuse. The cost and availability of fish antibiotics was recorded. The proportion of reviews and comments related to human consumption was calculated. Consumer review traffic based on "likes" and "dislikes" received was compared between human- and non-human consumption-related reviews. Selected fish antibiotics were purchased and evaluated for physical appearance and compared to FDA-approved available equivalents. We found 24 website vendors with online ordering available for OTC fish antibiotics. Cost varied significantly by antibiotic and quantity ranging from USD $8.99 to $119.99. There were 2,288 reviews documented for the 9 selected antibiotics being sold. Among consumer reviews, 2.4% were potentially associated with human consumption. Human consumption-related reviews constituted 30.2% of all "likes" received and 37.5% of all "dislikes" received. Human consumption-related reviews received an average of 9.2 likes compared to 0.52 likes for non-human consumption-related reviews. The 8 fish antibiotics purchased were consistent with FDA-approved equivalents in physical appearance. Although infrequent, antibiotics intended for fish use are being purchased online without a prescription for self-medication to circumvent professional medical care.

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Reviews related to human consumption generate significant online traffic compared to reviews unrelated to human consumption.

Introduction

Self-medication is defined as the use of over-the-counter (OTC) or prescription medication to treat self-diagnosed disorders, symptoms, or illnesses [1, 2]. Patient self-medication with antibiotics is an inappropriate medication utilization of medication that may produce unwarranted allergic reactions, drug interactions, adverse drug events, and excessive costs [3–5]. Furthermore, this inappropriate antibiotic use can prevent a correct diagnosis, allow for the spread of infection, delay appropriate therapy, and may contribute to antibiotic resistance [3–5]. Self-medication with antibiotics occurs across the globe, and has become a more common phenomenon in the United States (US) [1, 6–12]. A recent review indicated that the prevalence of nonprescription antibiotic use varied from 1% to 66%, depending on population characteristics studied [13].

The availability of OTC antibiotics without a prescription in some countries is a known contributing factor to self-medication. Recent systematic reviews indicate that antibiotics can be purchased without a prescription in many developing countries across the world, despite regulations prohibiting this practice [14, 15]. Online purchases have become an important source of antibiotics without a prescription in the US and United Kingdom (UK) as well [16, 17]. In 2017, 45% of online pharmacies in the UK sold antibiotics without a prescription, 80% of which required consumers to choose the antibiotic agents, dose, and quantity [17]. Another study found that 36.2% of antibiotics sold online in the US were sold without a prescription [16]. In the present COVID-19 era or in an analogous scenario with high rates of unemployment and quarantine restrictions, persons seeking antibiotics online may increase as some avoid in-person visits. Patients consuming antibiotics purchased online without a valid prescription are at additional risk of using the incorrect medication, dose, or duration as well as receiving a poor-quality product lacking official validation of contents.

Recent studies have shown that veterinarian-prescribed antibiotics or antibiotics intended solely for animal use have become a source for self-medication including among members of the US Armed Forces and some underrepresented ethnic communities [18, 19]. Zoorob and colleagues found that 4% of non-prescription antibiotics use were veterinarian-prescribed [19]. Access to these antibiotics intended for animal use appears to be more so driven by OTC availability in street-side businesses (i.e. pet stores) or online marketplaces. In contrast to antibiotics obtained for dogs and cats, the purchase of fish antibiotics in the US does not require pet prescription information, and the products are not FDA-regulated [20]. There are an estimated 13.1 million American households that own a pet fish, creating a significant market for fish medications [21]. In 2018, the FDA released a formal statement, "Ornamental Fish Drugs and You," to warn the public against utilizing medications intended for animal use. The statement highlights ornamental fish antibiotics have not been approved, conditionally approved, or indexed by the FDA, and the illegality of marketing them for human use [20]. The availability and use of fish antimicrobials was recently highlighted in the global news after a man in the US died from ingesting chloroquine phosphate for fish aquariums in an attempt to prevent COVID-19 [22].

The online availability of OTC fish antibiotics and the intent of consumers purchasing these antibiotics has not been quantified. The purpose of this study was to assess online

availability of OTC fish antibiotics and describe their intended use for self-medication through publicly available comments and product purchase reviews.

Materials and methods

The authors conducted a prospective, cross-sectional assessment of all website and online vendors selling fish antibiotics between August and September of 2019. The primary objective of this study was to identify the proportion of comments and reviews on online fish antibiotics associated with human consumption. The secondary objectives were to evaluate the traffic and attention received by reviews and comments associated with human consumption versus comments not associated with human consumption. Traffic and attention were measured by the number of reviews, "likes," and "dislikes" associated with each review/comment. Additionally, the authors sought to evaluate the physical appearance of commonly sought online fish antibiotics and compare them with FDA-approved equivalents. Using the Google® search engine and the key words "fish antibiotics" and "online (English only)," vendors and websites selling fish antibiotics were identified. Vendor websites were included if product information (e.g. pricing, quantity), consumer reviews, and comments were publicly available. Online vendors who do not provide shipment to the US were excluded. Other antimicrobials (e.g. antifungals) were not investigated. Investigators screened the fish antibiotics sold on every website and the top 9 antibiotics that could be commonly used for human consumption were determined. Of note, these antibiotics were officially sold for the intended treatment of ornamental fish and domestic fish tanks. The cost and quantity supplied of fish antibiotics was recorded. The reviews and comments left by consumers who purchased fish antibiotics were read and categorized as either related or unrelated to human consumption (Fig 1). To determine if possibly purchased for human consumption, the following criteria were used to evaluate reviews and comments: (a) Explicitly stated purchased antibiotics were for human consumption. (b) Suggested purchased antibiotics were used for self-medication in a concealed manner (e.g. to treat an infectious disease that only humans could have, purchased due to lack of medical insurance or can't afford the cost to see a doctor). (c) Suggested that fish antibiotics were the same as human antibiotics and can or should be used for humans. If the verbiage was ambiguous or non-descript (e.g. "The product worked great;" "worked as expected"), the comments were assumed to be non-human related. The proportion of reviews and comments related to human consumption was calculated. All online reviews were conducted by two investigators (PBB, ZW). Discordant reviews were discussed and allocated based on consensus. Eight fish antibiotics (sulfamethoxazole/trimethoprim, cephalexin, amoxicillin, metronidazole, penicillin, ciprofloxacin, clindamycin and doxycycline) were obtained and compared with FDA-approved human equivalents using a commercially available pill identification program (Lexicomp Inc®). One fish antibiotic (erythromycin) was not analyzed because fish erythromycins being sold were powder-formed and it was hard to compare them with FDA-approved equivalents using pill identification programs.

Statistical analysis

Descriptive statistics were used to estimate the prevalence of human related consumption. Data were checked for normality and t-test analyses were conducted to compare traffic between the human consumption-related and non-human consumption-related reviews.

Results

The authors identified 24 website vendors with online ordering available for OTC fish antibiotics. Nine vendor websites (S1 Table) were included and 15 websites were excluded due to the

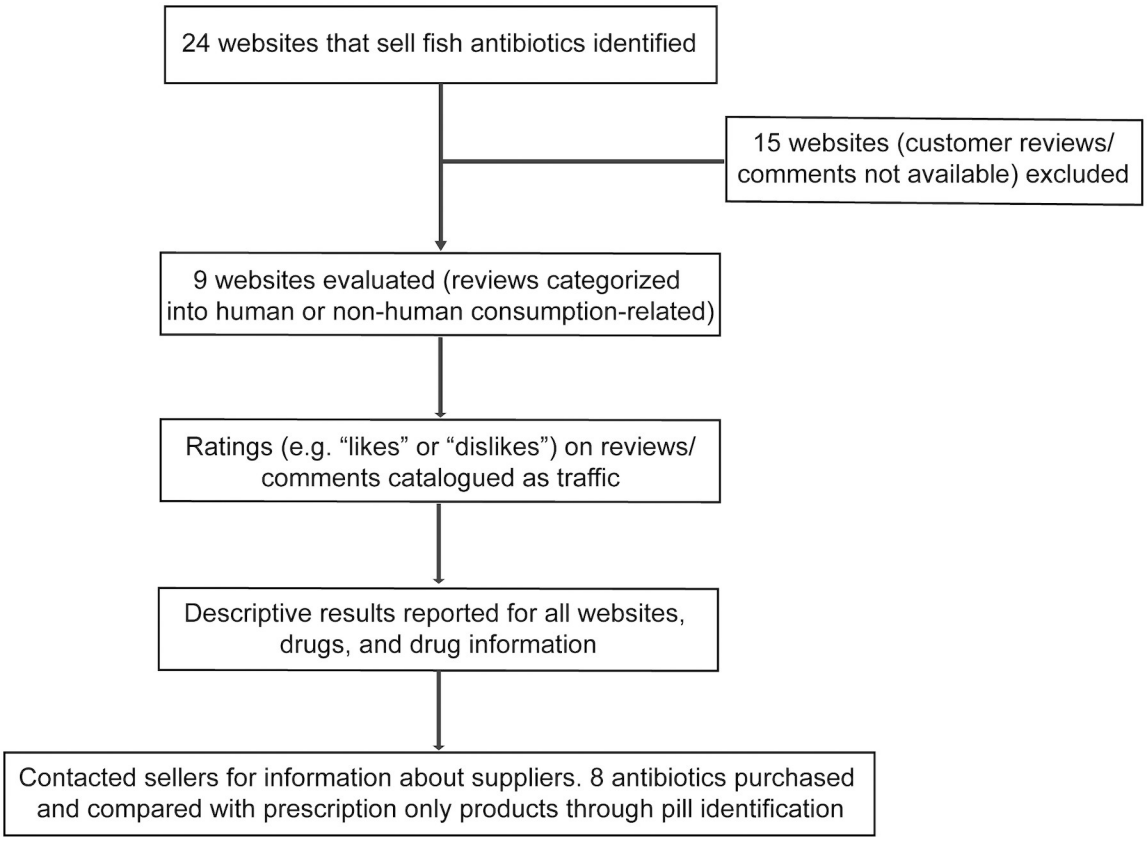

Fig 1. Study methodology.

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consumer reviews not existing or not being publicly available. Nine fish antibiotics were selected and analyzed based on their common use in the treatment of human infections and the possibility of having negative repercussions as a result of self-medication (Table 1).

As shown in Table 1, the cost of fish antibiotics varied significantly between antibiotics and quantities, ranging from $8.99 to $119.99. Consumer review traffic and proportion of reviews related to human consumption are shown in Table 2. There were 2,288 reviews documented

Table 1. Baseline information of 9 reviewed antibiotics.

Names of fish antibiotics	Numbers of the reviews	Price range (USD$)			
		Lowest price	Corresponding specifications	Highest price	Corresponding specifications
Amoxicillin	1314	8.99	250mg*30 Tab	75.6	4*500mg*100 Cap
Cephalexin	445	11.99	250mg*30 Cap	40.99	500mg*100 Cap
Metronidazole	229	13.99	500mg*12 Packets	89.99	500mg*100 Cap
Ciprofloxacin	89	27.99	250mg*30 Tab	119.99	500mg*100 Tab
Penicillin	91	13.49	250mg*30 Tab	54.99	500mg*100 Tab
Clindamycin	40	20.99	150mg*30 Cap	54.99	150mg*100 Cap
Doxycycline	36	19.99	100mg*12 Packets	99.99	100mg*100 Cap
Sulfamethoxazole, Trimethoprim	32	18.99	Sulfamethoxazole 800 mg/Trimethoprim 160 mg*30 Tab	42.99	Sulfamethoxazole 800 mg/Trimethoprim 160 mg*100 Tab
Erythromycin	12	19.99	250mg*12 Packets	54.99	250mg*60 Packets

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Table 2. Consumer reviews on fish antibiotics and proportion of reviews related to human consumption.

Fish antibiotic	Percentage of human consumption-related reviews, n_{hr}/n_{tr}[1](%)	Percentage of Likes among human consumption-related reviews, n_{hl}/n_{tl}[2] (%)	Percentage of Dislikes among human consumption -related reviews, n_{hd}/n_{td}[3] (%)
Amoxicillin	28/1314 (2.1)	405/1173 (34.5)	7/8 (87.5)
Cephalexin	12/445 (2.7)	6/121 (5.0)	0/6
Ciprofloxacin	3/89 (3.4)	24/66 (36.4)	0/0
Clindamycin	2/40 (5.0)	3/16 (18.8)	0/0
Doxycycline	1/36 (2.8)	0/10	0/0
Erythromycin	1/12 (8.3)	0/0	1/1 (100)
Metronidazole	5/229 (2.2)	67/260 (25.8)	1/8 (12.5)
Penicillin	3/91 (3.3)	1/12 (8.3)	0/1
Sulfamethoxazole, Trimethoprim	0/32	0/16	0/0
Total	55/2288 (2.4)	506/1674 (30.2)	9/24 (37.5)

[1] The percentage of human consumption-related reviews: the number of human consumption-related reviews (n_{hr})/the number of total reviews of the fish antibiotic (n_{tr}).

[2] The percentage of likes among human consumption-related reviews: the number of likes among human consumption-related reviews (n_{hl})/the total number of likes among all reviews (n_{tl}).

[3] The percentage of dislikes among human consumption-related reviews: the number of dislikes among human consumption-related reviews (n_{hd})/the total number of dislikes among all reviews (n_{td}).

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for the 9 selected antibiotics being sold. Among consumer reviews, 55 (2.4%) of them were potentially associated with human consumption. There was no statistical difference between the numbers of human consumption-related reviews and non-human consumption-related reviews ($p = 0.10$). Human-consumption related reviews constituted 30.2% of all "likes" received and 37.5% of all "dislikes" received among all reviews. Human consumption-related reviews received an average of 9.2 likes per review (55 reviews received 506 likes) compared to 0.52 likes per review (2,233 reviews received 1168 likes) for non-human related reviews. Fish antibiotics with a high percentage of human consumption-related reviews are as follows, erythromycin (8.3%), clindamycin (5%), ciprofloxacin (3.4%), penicillin (3.3%), and doxycycline (2.8%). Fish antibiotics with a high percentage of "likes" among human consumption-related reviews are as follows, ciprofloxacin (36.4%), amoxicillin (34.5%), and metronidazole (25.8%). Select reviews demonstrating potential human consumption are shown in Fig 2.

Among the 8 antibiotics purchased and compared to FDA-approved equivalents, all products were deemed consistent with human generic equivalents based on physical appearance. Chemical testing was not performed. Details regarding the physical products are available in Table 3 and Fig 3 (3a-3h). Erythromycin was not purchased because it was only available in a powder formulation.

Discussion

Reported self-medication with fish antibiotics documented in a viral tweet from 2017 drew significant market attention. The tweet directed readers to Amazon's online fish antibiotics with reviewer comments suggesting human consumption [23]. Amazon has since discontinued the sale of fish antibiotics, although antiparasitic and antifungal fish medications remain available for purchase at the time of this publication. In the present study, there were numerous readily available websites selling fish antibiotics online. The findings of this study confirm that fish antibiotics can be freely purchased online without prescription in the US. Though, as anticipated, most customers are assumed to have bought the fish antibiotics for pets, 2.4% (55/

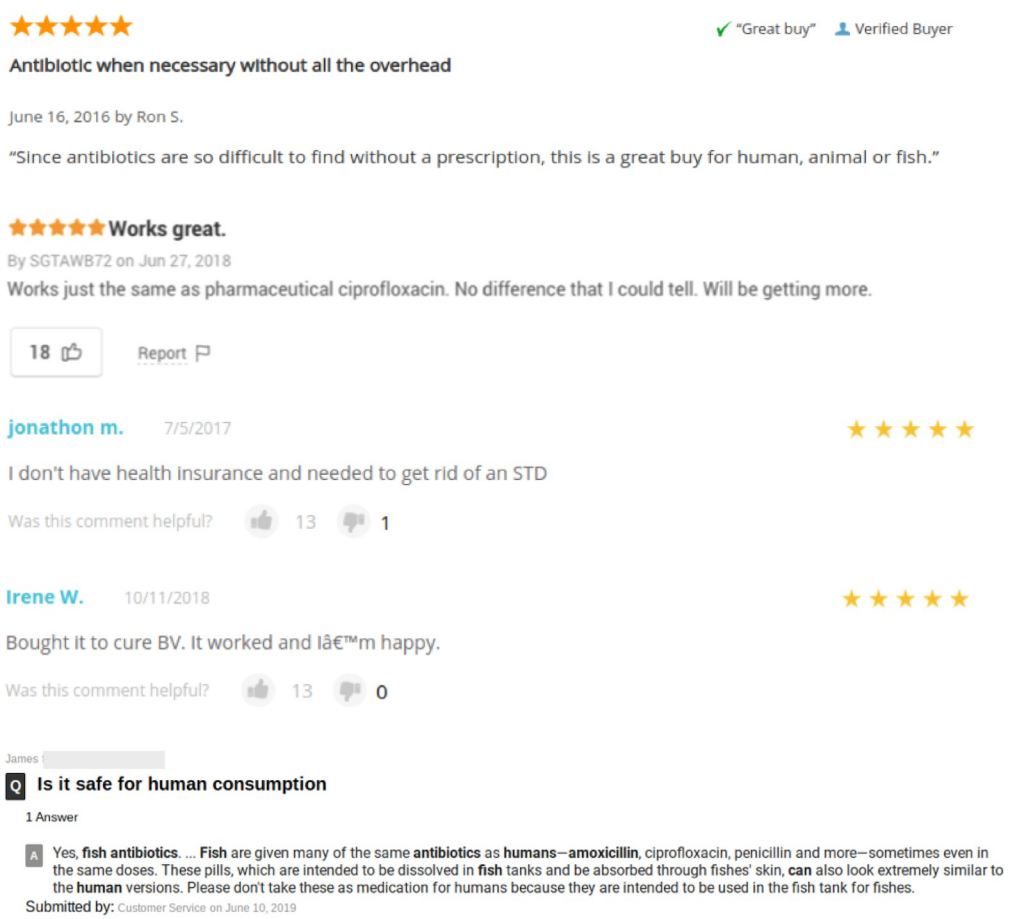

Fig 2. Reviews on self-medication with fish antibiotics.

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Table 3. General information of 8 purchased fish antibiotics.

Generic name	Distributor	NDC	ID conformed	Labeler
Metronidazole	Thomas Labs®	86024-017-30	Yes	BLUE POINT LABORATORIES, UNICHEM PHARMACEUTICALS
Clindamycin	Thomas Labs®	86024-003-30	Yes	MYLAN INSTITUTIONAL
Amoxicillin	Thomas Labs®	86024-011-30	Yes	SANDOZ
Cephalexin	Thomas Labs®	86024-006-30	Yes	ORCHIDPHARMA
Penicillin	Thomas Labs®	86024-015-30	Yes	AUROBINDO PHARMA, GREENSTONE, NORTHSTAR RX, RISING PHARMACEUTICALS
Sulfamethoxazole/ Trimethoprim	Goldman Pharmaceutical Group Inc.	NA	Yes	MYLAN INSTITUTIONAL
Ciprofloxacin	Thomas Labs®	86924-008-30	Yes	PHYSICIAN PARTNER
Doxycycline	Goldman Pharmaceutical Group Inc.	NA	Yes	AVKARE

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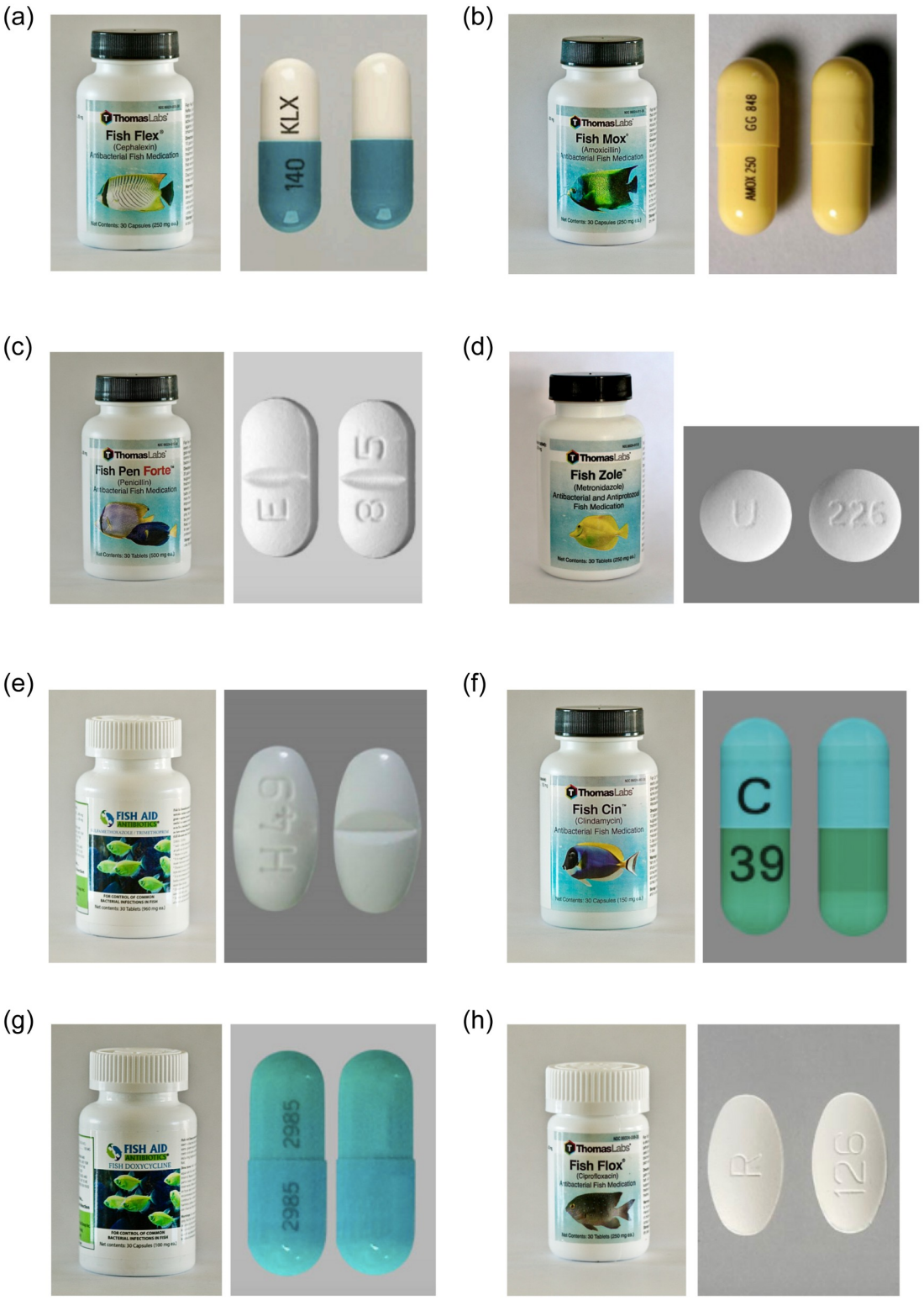

Fig 3. (3a-3h). Pill and capsule identification of 8 fish antibiotics. Fig 3a Generic Name: Cephalexin; Shape: oblong; Color List: green; white; Imprint Side 1: 140; Imprint Side 2: KLX; Strength Field Collection: 250mg; Dosage Form: Capsule; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3b Generic Name: Amoxicillin; Shape: oblong; Color List: yellow; Imprint Side 1: AMOX 250; Imprint Side 2: GG 848; Strength Field Collection: 250mg; Dosage Form: Capsule; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3c Generic Name: Penicillin V Potassium; Shape: oblong; Color

List: white; Imprint Side 1: E; Imprint Side 2: 8 5; Strength Field Collection: 500mg; Dosage Form: Tablet; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3d Generic Name: Metronidazole (Systemic); Shape: round; Color List: white; Imprint Side 1: U; Imprint Side 2: 226; Strength Field Collection: 250mg; Dosage Form: Tablet; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3e Generic Name: Sulfamethoxazole and trimethoprim; Shape: oval; Color List: white; Imprint Side 1: H 49; Strength Field Collection: Sulfamethoxazole 800 mg and trimethoprim 160 mg; Dosage Form: Tablet; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3f Generic Name: Clindamycin (Systemic); Shape: oblong; Color List: light blue; light green; Imprint Side 1: C; Imprint Side 2: 39; Strength Field Collection: 150mg; Dosage Form: Capsule; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3g Generic Name: Doxycycline; Shape: oblong; Color List: light blue; Imprint Side 1: 2985; Imprint Side 2: 2985; Strength Field Collection: 100mg; Dosage Form: Capsule; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source). Fig 3h Generic Name: Ciprofloxacin; Shape: oval; Color List: white; Imprint Side 1: R; Imprint Side 2: 126; Strength Field Collection: 250mg; Dosage Form: Tablet; Route List: Oral; Bioequivalence Rating: AB; Rx/OTC: Rx (multiple source).

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2,288) of online customers potentially used them for self-medication based on the comments and reviews left on the products. These human consumption-related reviews contributed to 30.2% (506/1,674) of all "likes" received and 37.5% (9/24) of all "dislikes" received. Although the percentage of human consumption associated reviews is low, these reviews generate significantly more traffic compared to other reviews and comments. A number of studies have shown that purchasing behavior, intentions, and attitudes towards products can be influenced by the consumer ratings and reviews [24–26], and the most important factors affecting sales and attitudes are the valence and the volume of reviews [25–27]. Another study indicated that when overall "likes" are high, consumers are more likely to have higher brand involvement and purchase intention than when overall "likes" are low [28]. Customer reviews are essential, as it is estimated that approximately 58% of Americans conduct research about the products and services prior to buying them [29]. This suggests that human-consumption related reviews may encourage more people to use antibiotics marketed for fish for self-medication. Some social media platforms and websites also reported people were using fish antibiotics as a cheap alternative for self-medication and showed that this issue was reaching the lay public [21, 23, 30, 31].

In analyzing these human consumption related reviews, the authors felt that, consistent with other literature, multiple factors may contribute to patient self-medication with antibiotics, including affordability of physician visits, convenience of ordering and delivery to home, embarrassment associated with potential diagnosis, and lack of knowledge of antibiotic use and misuse. Surprisingly, one vendor customer service agent publicly expressed that fish antibiotics can be used in humans. There are certainly many potential hazards of self-medicating with fish antibiotics. As stated in a report issued by the FDA in 2018 [20], the safety and effectiveness of the antibiotics that are available in pet stores, or online had not been evaluated and have not been approved by the FDA. Recently, the FDA also released a statement to warn the public not to use chloroquine phosphate intended for fish [32] as treatment for COVID-19 in humans because these products sold for aquarium use have not been evaluated by the FDA [33]. All 8 fish antibiotics purchased had consistent physical findings with FDA-approved equivalents using pill identification, which is something that has drawn online attention in the lay public among advocates for self-treating using fish antibiotics [23, 30, 31]. However, regardless of identical physical appearance, these fish antibiotics may not meet FDA's standards for purity and potency, and the handling and storage of these medications were unknown. The authors were unable to obtain further information regarding supply chain of the fish antibiotics from the vendors or suppliers.

Inappropriate use of antibiotics may cause a variety of adverse effects, including serious complications such as allergic reactions, organ dysfunction, or *Clostridioides difficile* infection [34–39]. Perhaps most concerning is that self-medication infers self-diagnosis, significantly increasing the risk for delayed, masked, or missed diagnoses [40]. This is largely concerning

among communicable diseases, such as sexually transmitted infections (STIs), that may lend themselves to self-medication. In the present study, several product reviews of metronidazole specifically alluded to management of STIs including trichomoniasis and bacterial vaginosis. Inappropriate use of antibiotics without medical guidance may also increase the risk of the selection of resistant bacteria [41, 42]. While using fish antibiotics for self-medication may not contribute on a large scale to antimicrobial resistance, it certainly may impact the individual who chooses to self-medicate. Antibiotic consumption may can also impact future antibiotic choice if the patient ultimately seeks care for a particular infection [43, 44].

Some strategies may be needed to decrease self-medication and account for this use. Efforts on continuing public awareness of rational use of antibiotics appears warranted and necessary. The Centers for Disease Control and Prevention advocates for antibiotic awareness among patients and providers to improve antibiotic use and combat continued emergence of antibiotic resistance [45]. Upon knowledge of self-medication, clinicians should strive to determine patient specific motivators for self-medication and barriers to seeking care. These simple interventions may have long-term benefits for the patient to perhaps enhance medication access for the patient or manage other underlying reasons for self-medication. Continued discussion around the availability of antibiotics without medical professional advice is also warranted.

There are several limitations to this study. Firstly, this study is based on available website transactions and reviews, and thus it may not represent all vendors selling fish antibiotics. Additionally, the proportion of human consumption related reviews may be under- or overestimated due to consumer reluctance to disclose use of fish antibiotics for self-medication. Finally, our study focused only on English language websites and thus some websites in other languages were excluded.

This study is the first to objectively document the prevalence of fish antibiotics intended for human self-medication. Future studies should evaluate objective motivators behind self-medication with fish or other OTC antibiotics. Quality assurance and verification of stated contents of fish antibiotics is currently underway.

Conclusions

Although infrequent, antibiotics intended for fish use are being purchased online without a prescription for self-medication to circumvent professional medical care. Reviews related to human consumption generate significant online traffic compared to reviews unrelated to human consumption. Patient education and clinician awareness of this phenomenon may help mitigate patient-specific utilization.

Supporting information

S1 Table. The list of websites included in the study.
(DOCX)

Author Contributions

Conceptualization: P. Brandon Bookstaver.

Data curation: Weiwei Zhang, P. Brandon Bookstaver.

Formal analysis: Weiwei Zhang, P. Brandon Bookstaver.

Investigation: Weiwei Zhang, Austin Williams, P. Brandon Bookstaver.

Methodology: Weiwei Zhang, Austin Williams, P. Brandon Bookstaver.

Project administration: Weiwei Zhang, P. Brandon Bookstaver.

Resources: Nicole Griffith, Jessica Gaskins.

Software: Austin Williams.

Supervision: P. Brandon Bookstaver.

Visualization: Nicole Griffith.

Writing – original draft: Weiwei Zhang.

Writing – review & editing: Weiwei Zhang, Nicole Griffith, Jessica Gaskins, P. Brandon Bookstaver.

References

1. Awad AEI, Matowe L, Thalib L. Self-medication with antibiotics and antimalarials in the community of Khartoum State, Sudan. J Pharm Pharm Sci. 2005; 8(2):326–331. PMID: 16124943
2. Organization WH. Guidelines for the regulatory assessment of medicinal products for use in self-medication. World Health Organization, 2000.
3. Carbon Claude, Bax RP. Regulating the use of antibiotics in the community. BMJ. 1998; 317 (7159):663–665. https://doi.org/10.1136/bmj.317.7159.663 PMID: 9728001
4. Hildreth Carolyn J., Burke Alison E., RM G. Inappropriate use of antibiotics. JAMA. 2009; 302(7):816. https://doi.org/10.1001/jama.302.7.816 PMID: 19690318
5. Nepal Gaurav, Bhatta S. Self-medication with antibiotics in WHO Southeast Asian Region: a systematic review. Cureus. 2018; 10(4):e2428. https://doi.org/10.7759/cureus.2428 PMID: 29876150
6. Grigoryan L, Haaijer-Ruskamp FM, Burgerhof JG, Mechtler R, Deschepper R, Tambic-Andrasevic A, et al. Self-medication with antimicrobial drugs in Europe. Emerg Infect Dis. 2006; 12(3):452–459. https://doi.org/10.3201/eid1203.050992 PMID: 16704784
7. Mitsi GJE, Basiaris H, Skoutelis A, Gogos C. Patterns of antibiotic use among adults and parents in the community: a questionnaire-based survey in a Greek urban population. International journal of antimicrobial agents. 2005; 25(5):439–443. https://doi.org/10.1016/j.ijantimicag.2005.02.009 PMID: 15848301
8. Hui P, Binglin C, Dangui Z, Jeremy F, Frieda L, William B.T, et al. Prior knowledge, older age, and higher allowance are risk factors for self-medication with antibiotics among university students in southern China. PloS one. 2012; 7(7):e41314. https://doi.org/10.1371/journal.pone.0041314 PMID: 22911779
9. Larson E, Grullon-Figueroa L. Availability of antibiotics without prescription in New York City. Journal of Urban Health. 2004; 81(3):498. https://doi.org/10.1093/jurban/jth133 PMID: 15273271
10. Larson EL, Dilone J, Garcia M, Smolowitz J. Factors which influence Latino community members to self-prescribe antibiotics. Nursing research. 2006; 55(2):94–102. https://doi.org/10.1097/00006199-200603000-00004 PMID: 16601621
11. Mainous AG III, Diaz VA, C M. Factors affecting Latino adults' use of antibiotics for self-medication. J Am Board Fam Med. 2008; 21(2):128–134. https://doi.org/10.3122/jabfm.2008.02.070149 PMID: 18343860
12. Mainous AG III, Cheng AY, Garr RC, Tilley BC, Everett CJ, McKee MD. Nonprescribed antimicrobial drugs in Latino community, South Carolina. Emerg Infect Dis. 2005; 11(6):883–888. https://doi.org/10.3201/eid1106.040960 PMID: 15963283
13. Grigoryan L, Germanos G, Zoorob R, Juneja S, Raphael JL, Paasche-Orlow MK, et al. Use of Antibiotics Without a Prescription in the US Population: A Scoping Review. Ann Intern Med. 2019; 171(4):257–263. https://doi.org/10.7326/M19-0505 PMID: 31330541
14. Sakeena MHF, Bennett AA, McLachlan AJ. Non-prescription sales of antimicrobial agents at community pharmacies in developing countries: a systematic review. Int J Antimicrob Agents. 2018; 52 (6):771–782. https://doi.org/10.1016/j.ijantimicag.2018.09.022 PMID: 30312654
15. Auta A, Hadi MA, Oga E, Adewuyi EO, Abdu-Aguye SN, Adeloye D, et al. Global access to antibiotics without prescription in community pharmacies: A systematic review and meta-analysis. J Infect. 2019; 78(1):8–18. https://doi.org/10.1016/j.jinf.2018.07.001 PMID: 29981773.

16. Mainous AG, Everett CJ, Post RE, Diaz VA, Hueston WJ. Availability of antibiotics for purchase without a prescription on the internet. Ann Fam Med. 2009; 7(5):431–435. https://doi.org/10.1370/afm.999 PMID: 19752471

17. Boyd SE, Moore LSP, Gilchrist M, Costelloe C, Castro-Sánchez E, Franklin BD, et al. Obtaining antibiotics online from within the UK: a cross-sectional study. J Antimicrob Chemother. 2017; 72(5):1521–1528. https://doi.org/10.1093/jac/dkx003 PMID: 28333179

18. Goff BJ, Koff JM, JA G. Obtaining antibiotics without a prescription. N Engl J Med. 2002; 347(3):223.

19. Zoorob R, Grigoryan L, Nash S, Trautner BW. Nonprescription antimicrobial use in a primary care population in the United States. Antimicrobial agents chemotherapy. 2016; 60(9):5527–5532. https://doi.org/10.1128/AAC.00528-16 PMID: 27401572

20. Administration USFD. Ornamental Fish Drugs and You. 2018 Aug 9 [cited 2019 Oct 21]. https://www.fda.gov/animal-veterinary/animal-health-literacy/ornamental-fish-drugs-and-you.

21. Association APP. Pet Industry Market Size & Ownership Statistics. 2019 [cited 2019 Oct 21]. https://www.americanpetproducts.org/press_industrytrends.asp.

22. Radio NP. Man Dies, Woman Hospitalized After Taking Form Of Chloroquine To Prevent COVID-19. 2020 Mar 24 [cited 2020 Mar 30]. https://www.npr.org/sections/coronavirus-live-updates/2020/03/24/820512107/man-dies-woman-hospitalized-after-taking-form-of-chloroquine-to-prevent-covid-19.

23. Sharp R. How bad is American healthcare? Read the reviews for aquarium antibiotics and decide for yourself. 2017 Jul 30 [cited 2019 Oct 27]. https://twitter.com/WrrrdNrrrdGrrrl/status/891643397009805312/photo/1?ref_src=twsrc%5Etfw%7Ctwcamp%5Etweetembed%7Ctwterm%5E891643397009805312&ref_url=https%3A%2F%2Fwww.smithsonianmag.com%2Fscience-nature%2Fhere-are-reasons-you-shouldnt-take-fish-antibiotics-180964523%2F.

24. Chen P-Y, Wu S-y, Yoon J. The impact of online recommendations and consumer feedback on sales. J ICIS Proceedings. 2004: 58.

25. Floyd K, Freling R, Alhoqail S, Cho HY, Freling T. How online product reviews affect retail sales: A meta-analysis. Journal of Retailing. 2014; 90(2):217–232.

26. King RA, Racherla P, Bush VD. What we know and don't know about online word-of-mouth: A review and synthesis of the literature. Journal of interactive marketing. 2014; 28(3):167–183.

27. Purnawirawan N, Eisend M, De Pelsmacker P, Dens N. A meta-analytic investigation of the role of valence in online reviews. Journal of Interactive Marketing. 2015; 31:17–27.

28. Phua J, Ahn SJ. Explicating the 'like'on Facebook brand pages: The effect of intensity of Facebook use, number of overall 'likes', and number of friends''likes' on consumers' brand outcomes. Journal of Marketing Communications. 2016; 22(5):544–559.

29. Jansen J. Online Product Research. 2010 Sep 29 [cited 2019 Oct 25]. https://www.pewinternet.org/2010/09/29/online-product-research/.

30. Ciechalskl S. Meet the people using fish antibiotics as a cheap alternative to American healthcare. 2017 Aug 6 [cited 2019 Oct 27]. https://mashable.com/2017/08/06/fish-antibiotics-america-healthcare/.

31. Wei-Haas M. This is why taking fish medicine is truly a bad idea. 2017 Aug 16 [cited 2019 Oct 27]. https://www.smithsonianmag.com/science-nature/here-are-reasons-you-shouldnt-take-fish-antibiotics-180964523/.

32. Smith SA. Fish Diseases and Medicine: CRC Press; 2019.

33. Administration USFD. FDA Letter to Stakeholders: Do Not Use Chloroquine Phosphate Intended for Fish as Treatment for COVID-19 in Humans. 2020 Mar 27 [cited 2020 Mar 30]. https://www.fda.gov/animal-veterinary/product-safety-information/fda-letter-stakeholders-do-not-use-chloroquine-phosphate-intended-fish-treatment-covid-19-humans.

34. Alshammari TM, Larrat EP, Morrill HJ, Caffrey AR, Quilliam BJ, Laplante KL. Risk of hepatotoxicity associated with fluoroquinolones: a national case–control safety study. Am J Health Syst Pharm. 2014; 71(1):37–43. https://doi.org/10.2146/ajhp130165 PMID: 24352180

35. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infect Dis. 2014; 14(1):13.

36. Hensgens MP, Goorhuis A, Dekkers OM, Kuijper EJ. Time interval of increased risk for Clostridium difficile infection after exposure to antibiotics. J Antimicrob Chemother. 2012; 67(3):742–748. https://doi.org/10.1093/jac/dkr508 PMID: 22146873

37. Kuster SP, Rudnick W, Shigayeva A, Green K, Baqi M, Gold WL, et al. Previous antibiotic exposure and antimicrobial resistance in invasive pneumococcal disease: results from prospective surveillance. Clin Infect Dis. 2014; 59(7):944–952. https://doi.org/10.1093/cid/ciu497 PMID: 24973312

38. Liu NW, Shatagopam K, Monn MF, Kaimakliotis HZ, Cary C, Boris RS, et al. Risk for Clostridium difficile infection after radical cystectomy for bladder cancer: analysis of a contemporary series. Urol Oncol. 2015; 33(12):503.e517–503.e522.

39. Torres MJ, Blanca M, Fernandez J, Romano A, De Weck A, Aberer W, et al. Diagnosis of immediate allergic reactions to beta-lactam antibiotics. Allergy. 2003; 58(10):961–972. https://doi.org/10.1034/j.1398-9995.2003.00280.x PMID: 14510712

40. Liu YC, Huang WK, Huang TS, Kunin CM. Inappropriate use of antibiotics and the risk for delayed admission and masked diagnosis of infectious diseases: a lesson from Taiwan. Arch Intern Med. 2001; 161(19):2366–2370. https://doi.org/10.1001/archinte.161.19.2366 PMID: 11606153

41. Thomas JK, Forrest A, Bhavnani SM, Hyatt JM, Cheng A, Ballow CH, et al. Pharmacodynamic evaluation of factors associated with the development of bacterial resistance in acutely ill patients during therapy. Antimicrob Agents Chemother. 1998; 42(3):521–527. https://doi.org/10.1128/AAC.42.3.521 PMID: 9517926

42. Guillemot D, Carbon C, Balkau B, Geslin P, Lecoeur H, Vauzelle-Kervroëdan F, et al. Low dosage and long treatment duration of β-lactam: risk factors for carriage of penicillin-resistant Streptococcus pneumoniae. JAMA. 1998; 279(5):365–370. https://doi.org/10.1001/jama.279.5.365 PMID: 9459469

43. DeMarsh M, Bookstaver PB, Gordon C, Lim J, Griffith N, Bookstaver NK, et al. Prediction of Sulfamethoxazole/Trimethoprim Resistance in Community-Onset Urinary Tract Infections. J Glob Antimicrob Resist. 2020; 21:218–222. https://doi.org/10.1016/j.jgar.2019.10.023 PMID: 31683038

44. Augustine MR, Testerman TL, Justo JA, Bookstaver PB, Kohn J, Albrecht H, et al. Clinical Risk Score for Prediction of Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae in Bloodstream Isolates. Infect Control Hosp Epidemiol. 2017; 38(3):266–272. https://doi.org/10.1017/ice.2016.292 PMID: 27989244

45. Prevention CfDCa. Antibiotic prescribing and use. 2019 Nov 15 [updated November 15, 2019; cited 2020 Mar 28]. https://www.cdc.gov/antibiotic-use/index.html.